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10/522,045	01/19/2005	Masashi Okamoto	10873.1576USWO	4002
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SHAW, AMANDA MARIE				
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/522,045

Applicant(s)

OKAMOTO ET AL.

Examiner

AMANDA SHAW

Art Unit

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Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 14 August 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1,4-12 and 14-26 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,4-12 and 14-26 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/S508)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

1. This action is in response to the amendment filed August 14, 2008. This action is made FINAL.

Claims 1, 4-12, and 14-26 are currently pending. Claim 1 has been amended.

Withdrawn Rejections

2. The rejections made under 35 USC 103(a) in sections 4-7 of the Office Action of May 14, 2008 are withdrawn in view of amendments made to the claims. However new rejections based on a different combination of prior art have been set forth below.

Claim Rejections - 35 USC § 112 2nd paragraph

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 4-12, and 14-26 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 4-12, and 14-26 are indefinite over the recitation of the phrase "wherein the collecting solution is poured into the centrifugation tube without separating the liquid phase part absorbed by the water absorbing resin particles from the water absorbing resin particles that have absorbed the liquid phase part". This phrase is considered unclear because there is no recitation in the claims that would lead one to believe that

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there are different phases (i.e. a liquid phase and a particle phase) in the centrifugation at the time the collection solution is poured into the centrifugation tube. Specifically the first step of the method requires that the water absorbing resin particles absorb substantially all of the liquid phase therefore at the time the collection solution is poured into the centrifugation tube there should only be one phase (i.e. a particle phase) in the centrifugation tube since substantially all of the water is absorbed.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 1, 4-8, 10-12, 14, and 25-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sato (US 2001/0009759) in view of Wardlaw (US Patent 2001/0033808), Lyman (US Patent 4683058 Issued 1987), and Tsuchiya (US Patent 57472747 Issued 1998).

Regarding Claim 1 Sato teaches a method of collecting a virus from a liquid sample using particles capable of being bound by viruses (Abstract). Sato teaches a method of bringing a liquid sample into contact with the particles which in one embodiment are hydrogel particles which absorb water (para 0074). Thus Sato teaches contacting liquid sample with water absorbing particles so that the liquid phase of the sample is absorbed by the water absorbing particles. Sato further teaches that the viruses are caught on the surface of the particles (para 0098). Thus Sato teaches that the viruses are caught on the surface of the water absorbing particles. Sato additionally teaches pouring a salt solution on the virus bound particles in order to disassociate viruses from the bound particles (para 0099). Thus Sato teaches contacting the water absorbing particles with a collecting solution so as to collect the microorganisms caught on the surface of the water absorbing particles. Regarding Claim 4 Sato teaches a method wherein a centrifugation is performed at 15000 rpm for 10 min (para 0141). Regarding Claim 7 Sato teaches that the hydrogel particles comprise a sulfonic acid monomer and water-soluble cross-linkable monomer (Para 0074). Thus Sato teaches a method wherein the water absorbing particles are hydrophilic cross-linked polymers having a hydrophilic function group. Regarding Claim 8 Sato teaches a method wherein the microorganism to be detected is hepatitis B virus (para 0140-0142). Regarding

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Claim 10 Sato teaches a method wherein the samples are derived from plasma, serum, cell lysate, urea, saliva and the like (para 0096). Regarding Claim 14 Sato teaches a method further comprising extracting the viral nucleic acids and then amplifying the nucleic acids (para 0099-0102). Regarding Claim 25 Sato teaches the nucleic acids are analyzed by PCR (para 0140-0142).

Sato does not teach that the water absorbing resin particles (i.e. hydrogels) absorb substantially all of the liquid in the liquid phase of the sample (clm 1). Further Sato does not teach a method wherein the collecting solution is contacted with the water absorbing particles without separating the water absorbing particles from the liquid phase (clm 1). Sato does not teach a method wherein the amount of the liquid sample is not greater than the water absorbing capacity of the water absorbing resin particles (clm 5). Sato does not teach a method wherein the amount to the collecting solution added is greater than a water absorbing capacity of the water absorbing resin particles that have absorbed the liquid phase part (clm 6). Sato does not teach a method wherein the amount of the liquid sample is in a range from 50 μ L to 500 μ L (clm 11) or in a range from 50 mL to 200 mL (clm 12).

However Wardlaw teaches hydrogels for collecting microorganisms. Wardlaw teaches that the amount of hydrogel required to collect microorganisms from a liquid sample is dependent on the amount of the liquid in the sample. Wardlaw further teaches that it is typically desired to use enough hydrogel so that essentially all of the water in the sample will be absorbed (Para 0011). Thus Wardlaw teaches water absorbing resin particles that absorb substantially all of the liquid phase of sample no

matter what size the liquid sample is. Further in instances where there is enough hydrogel to absorb essentially all of the water in the sample, one would not have to separate the water absorbing particles from the liquid phase prior to the collecting step for two reasons; (i) there would be nothing to separate because the water absorbing particles would have absorbed all of the liquid phase and (ii) the collection solution would not be absorbed by the water absorbing particles because the particles would be fully saturated from absorbing liquid in the sample.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Sato by using enough hydrogel particles to absorb essentially all of the liquid in the sample as suggested by Wardlaw (Para 0011). Using hydrogel particles capable of absorbing essentially all of the liquid in the sample would aid in the separation and purification of the virus from the sample. Further it would have been obvious to optimize the volume of the sample used to the amount of hydrogel or vice versa to achieve the best recovery of the microorganism. Additionally it would be obvious that the collection solution would not be absorbed by the water absorbing particles because the particles would be fully saturated from absorbing liquid in the sample.

Sato does not teach a method wherein the binding of the virus to the particles occurs on a planar filter supported so as to divide the centrifugation tube into an upper space and a lower space. Further Sato does not teach a method wherein during the centrifugation step the microorganisms accumulate at the bottom of the centrifugation tube.

However Lyman teaches a filter for a centrifuge tube. Specifically Lyman teaches a filter tube that is adapted to fit within the upper portion of a standard plastic centrifugation tube. The filter tube has a pressure filter at its lower end and an opening at its upper end for receiving liquids. When the filter tube is filled with a liquid sample comprising permeable and non permeable materials and the composite centrifuge tube and filter tube is spun in the centrifuge, the centrifugal force causes the permeable materials to flow through the filter and collect in the bottom of the centrifuge tube while the non permeable materials are retained in the filter tube (abstract). Thus Lyman teaches pouring a liquid sample into a centrifugation tube and centrifuging the sample so that permeable materials pass through the filter and accumulate at the bottom of the centrifugation tube. Additionally Lyman teaches the filter is made out of polycarbonate (col 4, line 8).

Tsuchiya provides guidance on properly choosing a filter with an appropriate pore size for detecting a particular microorganism (Column 3, lines 45-60). For example Tsuchiya teaches that in order to trap a small bacteria on a filter one could use a filter with a pore size of $0.2\mu\text{m}$. Therefore if you wanted that small bacteria to pass through the filter one could use a filter with a pore size larger than $0.2\mu\text{m}$.

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention to have modified the method of Sato and Wardlaw by performing the step of binding the virus to the particles on a filter in a centrifuge tube and then centrifuging the tube so that the virus accumulates at the bottom of the centrifugation tube as suggested by Lyman and Tsuchiya. In the method of Sato after the salt solution

is added, which makes the virus disassociate from the particles, one would be motivated to pass the salt solution and virus particles through a filter located in a centrifuge tube in order to collect the virus. Lyman teaches a composite filter tube and centrifuge tube that allows both separation by filtration through the tube into non permeable materials retained within filter tube and permeable materials collected in the centrifugation tube, and then the further separation of the permeable materials by specific gravity in the centrifuge tube (Column 4, lines 41-47). By placing a filter with the appropriate pore size based on the guidance provided by Tsuchiya in the centrifugation tube of Lyman one can control what size particles or microorganisms are considered permeable. Thus all of the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

6. Claims 9 and 16-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sato (US 2001/0009759) in view of Lyman (US Patent 4683058 Issued 1987) and Tsuchiya (US Patent 57472747 Issued 1998) as applied to claims 1, 8, and 14 above and in further view of Britschgi et al (US Patent 5726021 Issued 10-1998).

The teachings of Sato, Lyman and Tsuchiya are presented above.

Regarding Claim 9 the combined references not teach a method used to collect M. tuberculosis.

However Britschgi et al teach a method of detecting and characterizing different species of Mycobacterium such as *M. tuberculosis* (Column 6, lines 11-26). Britschgi teaches that the Mycobacterium are present either in a cell culture or from a clinical sample (Column 6, lines 27-28). Further Britschgi teach that the cells can be concentrated prior to lysis by centrifugation and filtration means (Column 7 lines 15-17). After lysis the cellular nucleic acid is extracted and amplified (Columns 8 and 9).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have used the method of Sato, Lyman and Tsuchiya for isolating *M. tuberculosis* from cultures before carrying out the nucleic acid extraction and amplification methods of Britschgi (Columns 8-9). An artisan would have been motivated to include the centrifugation step taught by Sato, Lyman and Tsuchiya in the method of Britschgi because such a step would have allowed for the removal of the cell culture media, cellular debris and other contaminants in the sample which could interfere with the nucleic acid analysis.

Regarding Claims 16-19, 21-22, and 24 the combined references do not teach a method further comprising (i) heating the sample to between 70 °C and 100°C; (ii) heating the sample for 1 to 30 min; (iii) heating the sample for 96°C for 10 min; (iv) using an extraction reagent with a pH between 7-12; (v) using a non ionic detergent; (vi) and using a metal chelating agent.

However Britschgi teaches a method for rapid and sensitive detection of Mycobacterium. The method comprises lysing the mycobacterium cells, extracting the nucleic acid from the lysed cells, and amplifying the lysed cells. Specifically Britschgi et

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al teach that cell lysis is completed by adding to the cell suspension a lysis reagent that contains a nonionic detergent (e.g. triton X which is a polyoxyethyleneglycol p-t-octylphenyl ether), and incubating the suspension at high temperatures. Britschgi et al further teach that the lysis solution typically has a pH between 6.5 and 10.5. The lysis buffer also preferably contains a chelating agent such as EDTA or EGTA. The cells are incubated in the lysis solution between 75°C-99°C until suitable lysis is observed. Typically incubation take 5 minutes or longer at 85°C. Following lysis the nucleic acids are further analyzed via PCR (Columns 8-9).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Sato, Lyman and Tsuchiya by examining the cellular constituents by performing nucleic acid analysis as suggested by Britschgi. Using nucleic acid analysis as a method to further examine cells collected from bodily fluids was routinely used in the art at the time of the invention as demonstrated by Britschgi et al and thus it would have been obvious to an ordinary artisan to have examined the collected cells using nucleic acid analysis.

Regarding Claims 20 and 23 the combined references do not teach (i) a method wherein the concentration of the nonionic detergent in the extraction reagent solution is in a range from 0.01 to 10 wt %; or (ii) a method wherein the concentration of the metal chelating agent in the extraction reagent solution is 0.1 to 100 mM.

However, determining the optimum conditions for performing nucleic acid lysis would have been obvious to one of ordinary skill in the art and well within the skill of the art. As discussed in MPEP 2144.05(b), "(w)here the general conditions of a claim are

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disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation. *In re Aller*, 220 F.2d 454, 105 USPQ 233, 235 (CCPA 1955).

MPEP 2144.05(b):

"Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955)"

"A particular parameter must first be recognized as a result-effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. *In re Antonie*, 559 F.2d 618, 195 USPQ 6 (CCPA 1977)."

7. Claim 15 is rejected under 35 U.S.C. 103(a) as being unpatentable over Sato (US 2001/0009759) in view of Lyman (US Patent 4683058 Issued 1987) and Tsuchiya (US Patent 57472747 Issued 1998) as applied to claim 14 above and in further view of Krupey (US Patent 5658779 Issued 8/1997).

The teachings of Sato, Lyman, and Tsuchiya are presented above.

The combined references do not teach a method wherein the elution solution is also the lysis solution.

However Krupey teaches a method wherein virus particles are captured on water insoluble particles. Krupey further teaches that the viruses may be desorbed from the particles using extraction agents (Column 12, line 45-47).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the method of Sato, Lyman, and Tsuchiya by using one solution to elute and lysis the virus as suggested by Krupey. Using solutions capable of eluting and lysing viruses at the same time are beneficial

because they save time by allowing the eluting and lysing steps to be performed simultaneously thus it would have been obvious to an ordinary artisan to have used such a solution in situations where it was desirable to collect a virus and used the virus for nucleic acid analysis.

Response To Arguments

8. The Applicants arguments in the response filed August 14, 2008 pertain to the newly presented rejections set forth in this office action.

The Applicants begin by summarizing the teachings of Sato and specifically state that Sato teaches a method wherein a liquid sample is added into a virus separating agent in an amount greater than the water absorbing capacity of the virus binding particles and that the liquid phase part of the sample is not fully absorbed by the particles. Then the Applicants state that Sato teaches a step of separating the virus binding particles which have virus adsorbed thereon from the liquid sample and a separate step of detaching the viruses from the virus binding particles. The Applicants point to the claims as amended which now require (i) that substantially all of the liquid phase is absorbed and (ii) that the viruses are detached from the virus binding particles without separating the virus binding particles from the liquid sample. The Applicants further state that neither Lyman nor Tsuchiya address these limitations.

This argument has been fully considered but is not persuasive. In the newly presented rejections a secondary reference (Wardlaw) has been applied to cure what is missing in Sato. Specifically Wardlaw teaches hydrogels for collecting microorganisms.

Wardlaw teaches that the amount of hydrogel required to collect microorganisms from a liquid sample is dependent on the amount of the liquid in the sample. Wardlaw further teaches that it is typically desired to use enough hydrogel so that essentially all of the water in the sample will be absorbed (Para 0011). Thus Wardlaw teaches water absorbing resin particles that absorb "substantially all" of the liquid phase of sample no matter what size the liquid sample is. Further in instances where there is enough hydrogel to absorb essentially all of the water in the sample, one would not have to separate the water absorbing particles from the liquid phase prior to the collecting step for two reasons; (i) there would be nothing to separate because the water absorbing particles would have absorbed all of the liquid phase and (ii) the collection solution would not be absorbed by the water absorbing particles because the particles would be fully saturated from absorbing liquid in the sample. Since Wardlaw clearly teaches a method wherein substantially all of the liquid phase is absorbed therefore allowing the viruses to be detached from the virus binding particles without separating the virus binding particles from the liquid sample, the combination of Sato and Wardlaw teach all of the new limitations present in the claims.

Conclusion

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

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§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amanda M. Shaw whose telephone number is (571) 272-8668. The examiner can normally be reached on Mon-Fri 7:30 TO 4:30. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached at 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Amanda M. Shaw
Examiner
Art Unit 1634

/Carla Myers/
Primary Examiner, Art Unit 1634